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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/635,433	08/10/00	NOE	PC10491A

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PAUL H GINSBURG
PFIZER INC
235 EAST 42ND STREET 20TH FLOOR
NEW YORK NY 10017-5755

EXAMINER	
MCKENZIE, T	
ART UNIT	PAPER NUMBER
1624	7

DATE MAILED: 06/27/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/635,433	NOE ET AL.	
	Examiner	Art Unit	
	Thomas C McKenzie,Ph.D.	1624	

-- The MAILING DATE of this communication appears on the cov r she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 May 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *1-15 and 21-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

1. This action is in response to amendments filed on 5/21/01. There are five pending claims under consideration. Claims 16-20 are use claims. The application concerns some piperidine and piperazine sulfonamides. This is the second action on the merits. All claims were previously rejected. Applicants have amended claim 16. This action is made non-final because new enablement, indefiniteness, and art rejections are made. Upon further consideration, the Examiner's analysis of the present claims as means plus function language interpreted according to 35 U.S.C. 112, sixth paragraph and thus, reading upon only the specific species present in the application is erroneous. Attempting to define means by function is not proper when the means can be clearly expressed in terms that are more precise.

Response to Amendment

2. Applicants" amendment to the first line of the specification claiming priority to Applicants' provisional application overcomes the objection made in point #6 of the previous office action. Applicants' amendment to claim 16, specifying that the small molecule has a molecular weight of 2000 or less overcomes the indefiniteness rejection concerning "small molecule" made in point #7.

Election/Restrictions

3. Claims 1-15 and 21-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Groups, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 6.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for small molecules of the formula I, does not reasonably provide enablement for all small molecules. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. Applicants' claims are drawn to the use of any molecule with a specific biological property. What are the structures of these molecules and where in the specification do Applicants teach how to make this potentially limitless structural variety of such molecules? Case law is clear that such broad claims lack sufficient supporting description. Starting with a hormone case which claimed a partially characterized peptide which was claimed in terms of its chemical properties, *In re Fisher*, 166 USPQ 18, U.S. Court of Customs and Patent Appeals wrote

> It is apparent that such an inventor should be allowed to dominate the future patentable inventions of others where those inventions were based in some way on his teachings. Such improvements, while unobvious from his teachings, are still within his contribution, since the improvement was made possible by his work. It is equally apparent, however, that he must not be permitted to achieve this dominance by claims which are insufficiently supported and hence not

> in compliance with the first paragraph of 35 U.S.C. 112. That paragraph requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved. In the present case we must conclude, on the record before us, that appellant has not enabled the preparation of ACTHs having potencies much greater than 2.3, and the claim recitations of potency of "at least 1" render the claims insufficiently supported under the first paragraph of 35 U.S.C. 112.

This concept was expanded by the U.S. Court of Appeals Federal Circuit in *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.* 18 USPQ2d 1016 in a case concerning EPO genes. Since genes were held to be chemicals, the principle regarding enablement applies as well to all small molecules. The court held that:

> A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and to describe how to obtain it. See *Oka*, 849 F.2d at 583, 7 USPQ2d at 1171. Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property, e.g., encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property. We hold that

> when an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the gene has been isolated.

These two cases were quoted with approval in *Genentech Inc v. The Wellcome Foundation Ltd.* , 31 USPQ2d 1161 by the U.S. Court of Appeals Federal Circuit, which added further in a concurring opinion "Such a claim, defining a substance only by its function, encompassing all substances that accomplish that result, is akin to a single means claim, which might fail to satisfy the definiteness requirement of 35 U.S.C Section 112. See *Fiers v. Sugano*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993)."

In *Fiers v. Sugano*, 25 USPQ2d 1601, U.S. Court of Appeals Federal Circuit repeated its views concerning the propriety of defining a chemical by it biological function and emphasized that for all chemicals including DNA "Claiming all DNA's that achieve a result without defining what means will do so is not in compliance with the description requirement; it is an attempt to preempt the future before it has arrived." They further required the inventor to have a "mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently

distinguish it. It is not sufficient to define it solely by its principal biological property."

Both *Fiers v. Sugano*, 25 USPQ2d 1601 and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.* 18 USPQ2d 1016 were quoted with approval by the U.S. Court of Appeals Federal Circuit in *Burroughs Wellcome Co. v. Barr Laboratories Inc.*, 32 USPQ2d 1915 who added, "An idea is definite and permanent when the inventor has a specific, settled idea, a particular solution to the problem at hand, not just a general goal or research plan he hopes to pursue. ... The conception analysis necessarily turns on the inventor's ability to describe his invention with particularity. Until he can do so, he cannot prove possession of the complete mental picture of the invention. These rules ensure that patent rights attach only when an idea is so far developed that the inventor can point to a definite, particular invention."

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "a medical condition of the

type characterized by the destruction of articular cartilage" is indefinite. The claims provide for the use of compounds, but the claims do not set forth any steps involved in determining how to identify "a medical condition of the type characterized by the destruction of articular cartilage". It is unclear what diseases and treatments applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how to practice this use. Must this pathology be the only one associated with the claimed disease? Must it be a major component of the disease process? Must the named pathology be a causative factor in the disease or are diseases that have "destruction of articular cartilage" as an indirect secondary effect also covered? Identifying which diseases applicants intend this claim to cover will involve extensive and potentially inconclusive clinical research. With out such clinical research to identify the patients and diseases applicants intend to treat, one skilled in the art cannot determine the metes and bounds of the claim. Hence, the claims are indefinite.

Applicants argue that one of ordinary skill in the art would understand the phrase and point to eight passages in the specification to clarify their meaning. Claiming treatment of the specific diseases which Applicants list in lines 2-4, paragraph 2, of page 4 of their amendment of 5/21/01 would overcome this rejection.

Applicants' argument is not persuasive for two reasons. Firstly, Stedman's Medical Dictionary (1995), does not list "destruction of articular cartilage". The medical school textbook "Cecil's Textbook of Medicine" has no listing in the index for the phrase. The standard reference work "The Merck Manual of Diagnosis and Therapy" also does not list the disease. Thus, the phrase "a medical condition of the type characterized by the destruction of articular cartilage" is not recognized in the art of medicine.

Secondly, the claim provides for the use of claimed compounds, but the claim does not set forth any steps involved in determining which diseases are "a medical condition of the type characterized by the destruction of articular cartilage". It is unclear which diseases include "a medical condition of the type characterized by the destruction of articular cartilage". Determining whether a given disease responds or does not respond to compounds active in Applicants' in vitro assays will involve undue experimentation. Suppose that a given drug, which has receptor antagonist properties *in vitro*, when administered to a patient with a certain disease, does not produce a favorable response. One can not conclude that specific disease does not fall within this claim. Keep in mind that:

A. It may be that the next patient will respond. No pharmaceutical has 100% efficacy. What success rate is required to conclude our drug is a treatment?

Thus, how many patients need to be treated? If "successful treatment" is what is intended, what criterion is to be used? If one person in 10 responds to a given drug, does that mean that the disease is treatable? One in 100? 1,000? 10,000? Will the standard vary depending on the current therapy for the disease?

B. It may be that the wrong dosage or dosage regimen was employed. Drugs with similar chemical structures can have markedly different pharmacokinetics and metabolic fates. It is quite common for pharmaceuticals to work and or be safe at one dosage, but not at another that is significantly higher or lower. Furthermore, the dosage regimen may be vital --- should the drug be given e.g. once a day, or four times in divided dosages? The optimum route of administration can not be predicted in advance. Should our drug be given as a bolus *iv* or in a time release *po* formulation. Thus, how many dosages and dosage regimens must be tried before one is certain that our drug is not a treatment for this specific disease?

C. It may be that our specific drug, while active *in vitro*, simply is not potent enough or produces such low concentrations in the blood that it is not an effective treatment of the specific disease. Perhaps a structurally related drug is potent enough or produces high enough blood concentrations to treat the disease in question, so that the first drug really does fall within the claim. Thus, how many

different structurally related receptor antagonists must be tried before one concludes that a specific compound does not fall within the claim?

D. Conversely, if the disease responds to our second drug but not to the first, both of whom are receptor antagonists *in vitro*, can one really conclude that the disease falls within the claim? It may be that the first compound result is giving the accurate answer, and that the success of second compound arises from some other unknown property which the second drug is capable. It is common for a drug, particularly in the CNS, to work by many mechanisms. The history of psychopharmacology is filled with drugs, which were claimed to be a pure receptor XYX agonist or antagonist, but upon further experimentation shown to effect a variety of biological targets. In fact, the development of a drug for a specific disease and the determination of its biological site of action usually precede linking that site of action with the disease. Thus, when mixed results are obtained, how many more drugs need be tested?

E. Suppose that our drug is an effective treatment of the disease of interest, but only when combined with some totally different drug. There are for example, agents in antiviral and anticancer chemotherapy which are not themselves effective, but are effective treatments when the agents are combined with something else.

Consequently, determining the true scope of the claim will involve extensive and potentially inconclusive research. Without it, one skilled in the art cannot determine the actual scope of the claim. Hence, the claim is indefinite.

6. Claims 16-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. What are the chemical formulas of the molecules whose use Applicants claim? The number of "small molecules having a molecular weight of under 2000 grams/mole is infinite.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 16-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Robinson ('361). The passage spanning line 66, column 1 to line 6 column 2 of this reference teaches aggrecanase inhibitory activity. Claim 15 of the reference lists treatment of specific diseases, which include Applicants' limitation "destruction of articular cartilage".

8. Claims 16-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Reiter ('392). Lines 1-8, column 1 of this reference teaches aggrecanase inhibitory activity. Claim 7 of the reference lists treatment of specific diseases, which include Applicants' limitation "destruction of articular cartilage".

9. Claims 16-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Duan ('336). Lines 43-46, column 238 of this reference teaches aggrecanase inhibitory activity. Claims 9-12 of the reference lists treatment of general diseases, which include Applicants' limitation "destruction of articular cartilage".

Conclusion

10. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (703) 308-9806. The FAX number for the Examiner is (703) 746-3152. The Examiner is available from 8:30 to 5:30, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mukund Shah can be reached on (703) 308-4716. Please direct general inquiries or any inquiry relating to the status of this application to the receptionist whose telephone number is (703) 308-1235.

John M. Ford
Senior Patent Examiner
Art Unit 1624

TCMcK
June 26, 2001

JOHN M. FORD
PRIMARY EXAMINER
GROUP ~~1600~~ 1624

1624